PRE-APPEAL BRIEF REQUEST FOR REVIEW

Applicant	:	Schor et al.
Appl. No.	:	09/581,651
Filed	:	October 10, 2000
For	:	POLYPEPTIDES, POLYNUCLEOTIDES AND USES THEREOF
Examiner	:	Rawlings, S.
Group Art Unit	:	1643

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicant requests review of the non-final rejection mailed on December 7, 2006 in the above-identified application. No amendments are being filed with this request. Review of the above-identified application is requested for the following reasons:

Priority/written description/new matter

The Examiner has maintained the rejection of Claims 1, 7-9, and 60 under 35 USC §112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner alleges that claims 1, 7-9, and 60 are only entitled to a "filing date" of the present application (10 December 2000). However, this date is not the "filing date" of the application. This application is the US National Phase of a PCT Application with an international filing date of December 15, 1998. The date referred to by the Examiner is simply the "371(c) date" that represents the "Date of Completion of all 35 U.S.C. **371** Requirements." M.P.E.P. 1893.03(b). According to this section of the MPEP "it should be borne in mind that the filing date of the international stage application is also the filing date for the national stage application. Specifically, **35 U.S.C. 363** provides that

> An international application designating the United States shall have the effect, from its international filing date under Article 11 of the treaty, of a national application for patent regularly filed in the Patent and Trademark Office except as otherwise provided in section **102(e)** of this title.

Thus, even if the present claims were limited to the filing date of the present application, that filing date would be December 15, 1998. *See*, *Id.* The only exceptions to the general rule that the

filing date is the PCT filing date relate to the availability of the application or patent granted thereon as prior art under § 102(e) and the availability of patent term adjustment. *Id*

The Examiner believes that although the prior specifications describe polynucleotides encoding a polypeptide comprising SEQ ID NO: 2, they do not describe the far broader genus of polynucleotides encoding polypeptides comprising SEQ ID NO: 41. The Examiner also contends that this language does not find support in the present specification, and considers it to be new matter. However, these conclusions are contrary to the Written Description Guidelines set forth in M.P.E.P. 2163.

The Written Description Guidelines (Example 14) acknowledge that a claim directed to homologues having "at least 95% sequence identity" to a specific sequence and having a specific activity is generally supported by a description of that specific sequence. Claims 1 and 9 recite that the polynucleotide has at least 95% sequence identity with the polynucleotide encoding the polypeptide comprising SEQ ID NO: 2. Support for this amendment can be found in the PCT application as filed (page 9, lines 13-19), as well as in the priority application No. GB 9726539.1, filed December 16, 1997 (page 9, lines 19-25) (see also Substitute Specification as filed June 3, 2005, on page 9, lines 6-12). Both specifications define variants of the polynucleotide of the invention as having relatively short stretches having preferably at least 95% homology (i.e. 95% identity) with equivalent stretches of the polynucleotide of the invention even though the overall homology between the two polynucleotides may be much less. Thus, one of ordinary skill in the art would recognize that the overall percent identity may also be as high as at least 95%. Furthermore, the functional assay allowing the determination of the migration stimulation factor activity of the polypeptide encoded by the claimed polynucleotide is well known in the prior art and is described in detail in Gray et al. (1989 *PNAS USA* 86:2438-2442) cited in the Specification as filed and incidentally co-authored by the present inventors, as well as in Picardo et al. (1991 *Lancet* 337:130-133), also cited in the Specification as filed.

Therefore, just as in Example 14 of the Written Description Guidelines, here there is actual reduction to practice of the single disclosed species. The Specification indicates that the genus of nucleic acids encodes the genus of proteins that must be variants of SEQ ID NO: 2 which do not have substantial variation since all of the variants must possess the specified activity, and all members of the genus of the nucleic acids have at least 95% identity to the disclosed species. Therefore, the disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description of the claimed invention.

Therefore, Claims 1, 7-9, and 60 are fully supported by the Specification of priority application GB 9726539.1 as filed on December 16, 1997 (page 9, lines 19-25, and page 23, lines 20 and 25-26), and they do not contain new matter.

The Examiner further required that the Applicant points to specific passages in the Specification which support the limitation regarding polypeptides having at least 30% of the ability of a polypeptide comprising SEQ ID NO: 2 to stimulate migration of adult skin fibroblasts into a collagen gel. Support for such limitation can be found in the PCT application as filed on page 10, lines 15-17 and page 20, lines 25-26 (see also Substitute Specification of the present application at page 10, lines 7-9, and page 20, lines 6-7).

Therefore, Claims 1, 7-9, and 60 are fully supported by the Specification as filed and their rejection under 35 USC §112, first paragraph should be withdrawn.

Enablement

The Examiner has maintained the rejection of Claims 1, 7-9, and 60 under 35 USC §112, first paragraph, as non-enabled, because the Specification allegedly does not describe an association between SEQ ID NO: 2 and the ability of a polypeptide comprising this amino acid sequence to stimulate migration of adult skin fibroblasts into a collagen gel, and the skilled artisan cannot predict which of the polypeptides comprising SEQ ID NO: 2 might have such activity.

> To be enabling, the specification of a patent must teach those skilled in the art to make and use the full scope of the claimed invention without 'undue experimentation' ... Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." *See In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993).

In the present case, the skilled artisan does not have to rely on predictions or undue experimentation. The Specification recites several passages establishing that a method of detecting migration stimulation factor activity of a polypeptide was known in the art at the time this invention was made (see, e.g. Gray et al. 1989 *PNAS USA* 86:2348-2442; and Picardo et al. 1991 *Lancet* 337:130-133). Therefore a skilled artisan armed with this knowledge will be able to experimentally test any number of polypeptides as described in Claim 1. Such experimentation would be far from undue or unreasonable as nothing more than carrying out the well-known experimental procedures would be required.

Therefore, Applicant asserts that Claims 1, 7-9, and 60 are fully enabled by the Specification as filed, and their rejection under 35 USC §112, first paragraph should be withdrawn.

Non-obviousness

The Examiner has maintained the rejection of Claims 1, 7-9, and 60 under 35 USC §103(a) as being allegedly unpatentable over Grey et al. (1989 *PNAS USA* **86**:2438-2442), as evidenced by

Schor et al. (*Breast Cancer Res.* 2001 3:373-379), GenBank™ Accession No. AJ276395, and UniProtKB/SwissProt™ Accession No. P02751, in view of Bendig (of record). Specifically, the Examiner has maintained that the 70 kDa polypeptide designated "MSF", which was isolated from cultured fibroblasts by Grey et al. is the polypeptide of SEQ ID NO: 2. The Examiner concluded that it would have been obvious to one of ordinary skill in the art at the time the invention was made to have cloned a nucleic acid molecule encoding the polypeptide isolated by Grey et al.

According to the MPEP:

> To establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must reference must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Here, the cited art either taken alone or in combination, fails to provide any of the elements of a *prima facie* case. The Examiner based his rejection on an allegation that the prior art would suggest the amino acid sequences encoded by the claimed polynucleotides, and that the polynucleotide sequences could be derived from these amino acid sequences. Applicant has previously argued that such reliance is legally improper. However, it is not necessary to resolve this legal issue in order to determine the nonobviousness of the presently pending claims. This is because the prior art simply does not disclose or suggest any of the amino acid sequences that are recited as being encoded by the claimed polynucleotides.

The cited Grey et al. reference discloses no sequence information at all, and provides no suggestion that the protein disclosed therein has the sequence of SEQ ID NO:2 much less the portion of SEQ ID NO:2 that is represented as SEQ ID NO:41. The examiner relied on the Schor et al. reference as evidence that the protein disclosed in Grey et al. had the sequence of SEQ ID NO:2. However, nothing in the Schor et al. paper implies anything about which protein was disclosed in the Grey et al. reference. The presence of overlapping authors in the two papers does not imply that the proteins disclosed in the Grey et al. paper were even discussed in the Schor et al. paper. In fact, there is absolutely no basis to conclude that the protein discussed in the Grey et al. reference has the sequence of SEQ ID NO:2.

GenBank™ Accession No. AJ276395 protein sequence was submitted by the inventor on March 6, 2000, which is after the international filing date of the present application, and thus does not constitute prior art. Thus, this reference cannot be relied upon in formulating the present rejection.

UniProtKB/SwissProt™ Accession No. P02751 sequence is that of a fibronectin precursor protein which does not have the sequence of SEQ ID NO:2, and does not comprise the sequence of SEQ ID NO: 41. Thus, this Accession No. provides no indication of the amino acid sequences recited in the claim as being encoded by the claimed polynucleotides.

Thus, none of the references that actually qualify as prior art disclose or suggest the amino acid sequences recited as encoded by the claimed polynucleotides. Thus, the legal principle of whether a genus of polynucleotide sequences can be rendered obvious by an amino acid sequence is not relevant to the present determination. Because the prior art does not suggest the amino acid sequences recited in the claim, it in no way can suggest the claimed polynucleotides. Based on the sequence of fibronectin precursor or the functional characteristics of the purified MSF of Gray there was no way to predict a polynucleotide sequence that would encode *inter alia* the amino acid sequence of SEQ ID NO: 41.

Novelty

The Examiner has maintained the rejection of Claims 1, 7-9, and 60 under 35 USC §102(b) as being allegedly anticipated by WO 99/31233A1. However, this document is actually the international publication of the present application after it was filed as PCT application No. PCT/GB98/03766. The publication did not occur until after the filing of the application. As such, it does not qualify as prior art and cannot anticipate itself.

Conclusion

None of the rejections set forth in the final Office Action can be sustained. Reconsideration and withdrawal of these rejections is respectfully requested.

Respectfully submitted,

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Dated: April 9, 2007

By: _____

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